Full length article

Per- and polyfluoroalkyl substances (PFAS) in United States tapwater: Comparison of underserved private-well and public-supply exposures and associated health implications

Kelly L. Smalling [a,*], Kristin M. Romanok [a], Paul M. Bradley [b], Mathew C. Morriss [c], James L. Gray [d], Leslie K. Kanagy [d], Stephanie E. Gordon [e], Brianna M. Williams [a], Sara E. Breitmeyer [a], Daniel K. Jones [c], Laura A. DeCicco [f], Collin A. Eagles-Smith [g], Tyler Wagner [h]

[a] *U.S. Geological Survey, Lawrenceville, NJ, USA*
[b] *U.S. Geological Survey, Columbia, SC, USA*
[c] *U.S. Geological Survey, West Valley City, UT, USA*
[d] *U.S. Geological Survey, Lakewood, CO, USA*
[e] *U.S. Geological Survey, Kearneysville, WV, USA*
[f] *U.S. Geological Survey, Madison, WI, USA*
[g] *U.S. Geological Survey, Corvallis, OR, USA*
[h] *U.S. Geological Survey, Pennsylvania Cooperative Fish and Wildlife Research Unit, The Pennsylvania State University, University Park, PA, USA*

ABSTRACT

Drinking-water quality is a rising concern in the United States (US), emphasizing the need to broadly assess exposures and potential health effects at the point-of-use. Drinking-water exposures to per- and poly-fluoroalkyl substances (PFAS) are a national concern, however, there is limited information on PFAS in residential tapwater at the point-of-use, especially from private-wells. We conducted a national reconnaissance to compare human PFAS exposures in unregulated private-well and regulated public-supply tapwater. Tapwater from 716 locations (269 private-wells; 447 public supply) across the US was collected during 2016–2021 including three locations where temporal sampling was conducted. Concentrations of PFAS were assessed by three laboratories and compared with land-use and potential-source metrics to explore drivers of contamination. The number of individual PFAS observed ranged from 1 to 9 (median: 2) with corresponding cumulative concentrations (sum of detected PFAS) ranging from 0.348 to 346 ng/L. Seventeen PFAS were observed at least once with PFBS, PFHxS and PFOA observed most frequently in approximately 15% of the samples. Across the US, PFAS profiles and estimated median cumulative concentrations were similar among private wells and public-supply tapwater. We estimate that at least one PFAS could be detected in about 45% of US drinking-water samples. These detection probabilities varied spatially with limited temporal variation in concentrations/numbers of PFAS detected. Benchmark screening approaches indicated potential human exposure risk was dominated by PFOA and PFOS, when detected. Potential source and land-use information was related to cumulative PFAS concentrations, and the number of PFAS detected; however, corresponding relations with specific PFAS were limited likely due to low detection frequencies and higher detection limits. Information generated supports the need for further assessments of cumulative health risks of PFAS as a class and in combination with other co-occurring contaminants, particularly in unmonitored private-wells where information is limited or not available.

1. Introduction

The quality and sustainability of drinking-water are rising concerns

in the United States (US) because of population-driven water demands, increasing contamination of drinking-water resources, and a growing understanding of potential human-health consequences associated with

exposures to contaminants. Per- and poly-fluoroalkyl substances (PFAS), "forever chemicals," are a class consisting of thousands of substances (Glüge et al., 2020) that are national/global human-health concerns due to environmental prevalence and persistence, toxicity, and human exposures through water and food (Evich et al., 2022; Sunderland et al., 2019; Tokranov et al., 2021). Legacy long-chain perfluoroalkyl acids (PFAAs) include perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), which are historically two of the most widely used and studied chemicals in the PFAS group (Tokranov et al., 2021). Due to their persistence, toxicity and bioaccumulation potential, actions have been taken voluntarily by industries and regulators worldwide to reduce the release of PFAAs including PFOA, PFOS and perfluorohexane sulfonic acid (PFHxS) (Butenhoff et al., 2009; Wang et al., 2015; Wang et al., 2013). Legacy PFAAs have been replaced by shorter chain analogues (C3-C6) such as perfluorobutanoic acid (PFBA), perfluorobutane sulfonic acid (PFBS), and perfluorohexanoic acid (PFHxA) as well as perfluoroether carboxylic acids (Bao et al., 2018; Li et al., 2020; Wang et al., 2015). These replacement PFAS are considered less bioaccumulative but still have the potential to persist in the environment and are quickly becoming the dominant PFAS in aquatic ecosystems (Wang et al., 2015; Wang et al., 2013). For example in chemical and product manufacturing in the US, two of the replacement products for PFOA and PFOS are the hexafluoropropylene oxide dimer acid (HFPO-DA or GenX) and PFBS, respectively (U.S. Environmental, 2022a).

PFAS are also widely-documented in human plasma (Hu et al., 2019) and can be maternally transferred pre- and post-natal (Bach et al., 2016; Blake and Fenton, 2020). Some PFAS have also been linked with human developmental, metabolic, and immune disorders as well as certain types of cancers (Barry et al., 2013; Grandjean and Budtz-Jørgensen, 2013; Liu et al., 2018). Potential pathways to drinking-water resources are diverse, including biosolids application, outdoor products (e.g., ski waxes), industrial releases, firefighting foams, and discharges from wastewater treatment, septic, stormwater, and landfill systems (Houtz et al., 2013; Kurwadkar et al., 2022; Masoner et al., 2019; Masoner et al., 2020; Salvatore et al., 2022; Sims et al., 2022). PFAS have been detected globally in surface and groundwater drinking–water resources (Evich et al., 2022) and in public drinking–water supplies prior to distribution (Andrews and Naidenko, 2020; Domingo and Nadal, 2019; Hu et al., 2016; McMahon et al., 2022).

In the US, publicly–available large national (e.g., U.S. Environmental Protection Agency's Third Unregulated Contaminant Monitoring Rule (UCMR3) (U.S. Environmental Protection Agency, 2022b) and state-specific databases comprise results from samples collected from public drinking-water treatment plants after treatment and prior to distribution, an approach which does not account for distribution-system changes that can affect consumer exposures at the tap (e.g., (Chen et al., 2019; Li et al., 2022; Mohammadi et al., 2022). Currently, limited information exists on drinking-water PFAS concentrations at the point of exposure (i.e., point-of-use tapwater) in public-supply and especially in unregulated and generally unmonitored private-wells. Private-well owners make up about 13–14% of the US population (Dieter et al., 2018) and previous research has documented a range of contaminant concerns in unregulated/unmonitored private-well drinking-water (Bradley et al., 2021a; Charrois, 2010; Focazio et al., 2006). Because the burden of private-well maintenance and monitoring falls on the owner (U.S. Environmental Protection Agency, 2023c), private-well water quality information remains scarce and typically is limited to only a few contaminants (e.g., coliform bacteria), due to high analytical costs, confusion of aesthetic quality (taste, odor) with safety, and a range of socioeconomic factors (Seltenrich, 2017; Zheng and Flanagan, 2017). This circumstance leads to the increased probability of unrecognized contaminant exposures (Zheng and Flanagan, 2017) and adverse health effects to private-well dependents (American Academy of Pediatrics, 2009) and illustrates the continued need for comparable assessments in both private-wells and public-supply at the point-of-use. For PFAS, such assessments are essential for quantifying population-level drinking-water exposures, identifying at-risk or contaminated water sources or systems, and determining potential human-health implications, especially for vulnerable subpopulations (Andrews and Naidenko, 2020).

PFAS regulations are changing rapidly in the US as a growing number of increasingly strict state and federal drinking-water guidelines/benchmarks have been established over the last 20 years (Interstate Technology Regulatory Council, 2022; Post, 2021; U.S. Environmental Protection Agency, 2023b). However, there currently are no final enforceable national drinking-water standards (e.g., maximum contaminant level [MCL]) for PFAS in the US and some states over the last few years have adopted their own enforceable MCLs for several PFAS (Interstate Technology Regulatory Council, 2022). In March 2023 U.S. Environmental Protection Agency (EPA) released, for public comment, proposed MCLs of 4 ng/L and MCLGs (maximum contaminant level goal) of zero for PFOA and PFOS. MCLGs are non-enforceable health goals established to protect vulnerable subpopulations irrespective of treatment technology, cost, and limits of detection. Further, any contaminant considered a likely or known carcinogen receives an MCLG of zero (U.S. Environmental Protection Agency, 2023b). A hazard index approach was also proposed to regulate PFHxS, GenX, PFNA, and PFBS. This approach considers the health-based values for PFHxS (9 ng/L), GenX (10 ng/L), PFNA (10 ng/L), and PFBS (2000 ng/L) to determine if the combined individual hazard quotient values pose a potential risk (U.S. Environmental Protection Agency, 2023b; U.S. Environmental Protection Agency, 2020). Significant shifts in guidelines to be more stringent are due primarily to improved information on potential health effects and exposure of sensitive subgroups such as infants through drinking-water (Post, 2021) indicating the need for more robust regional and national assessments of drinking-water with an emphasis on downstream exposure at the point-of-use especially as new proposed MCLs are promulgated in the US.

The U.S. Geological Survey (USGS) has been conducting ongoing national research on the potential for human exposures (both home and workplace) from natural and man-made tapwater contaminants, including PFAS (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2023a; Bradley et al., 2021a; Bradley et al., 2021b; Bradley et al., 2023b). To better understand human exposure to PFAS at the point-of-use, we conducted a standardized analytical survey of PFAS nationally using a network of volunteers and combined this new data with tapwater samples collected previously by our research team to maintain consistency in data collection/processing. The overall objectives of the study were to (1) directly compare PFAS exposure in regulated public-supply tapwater to tapwater from unregulated private-wells, (2) provide information on potential aggregated human-health effects of PFAS using health-based screening tools, and (3) identify potential landscape-scale drivers of PFAS contamination in tapwater.

2. Material and methods

2.1. Site selection and sample collection

This nationwide pilot assessment included 716 tapwater samples collected from residences, businesses, and drinking-water treatment plants across the US (Figure S1) from 2016 to 2021. Of these, 409 tapwater samples were collected at the point-of-use in 2021 from 155 unregulated private–well and 252 regulated public–supply locations in all 50 states, the District of Columbia, Puerto Rico, and the US Virgin Islands (Fig. 1, Figure S1) using a network of volunteers. Sampling locations were selected based on a presumptive–impact gradient approach wherein we identified locations in low (leveraged National Park Service/US Fish and Wildlife Service colleagues/sites), median (general outreach to colleagues and community volunteers, etc.), and high (targeted samples near reported PFAS sources based on geospatial information) human–impacted areas. Three locations (2 private-wells and 1 public-supply) were also sampled repeatedly (0, 0.5, 6, 12 and 24 h on day 1, daily for 7 days and then at least weekly for up to 2 months) to
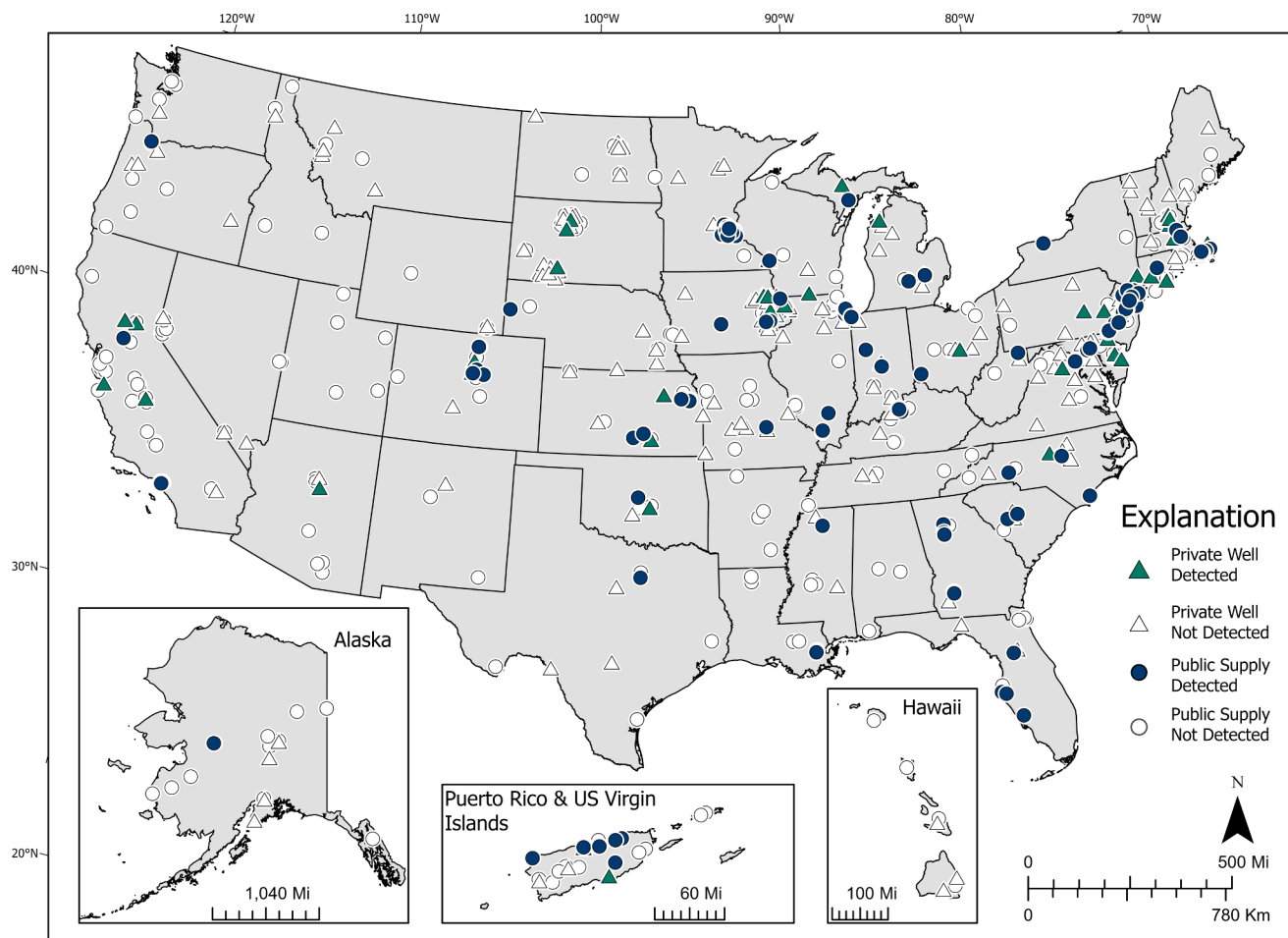
Fig. 1. Per- and polyfluoroalkyl substances (PFAS) detections in point-of-use tapwater collected from public-supply (blue circles) and private-wells (green triangles) across the United States including Puerto Rico and the U.S Virgin Islands. Samples with no detections are represented by open circles (public-supply) and triangles (private-wells). Tapwater samples were collected from 716 locations from 2016 to 2021. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

assess temporal changes in PFAS concentrations and profiles. Each volunteer was shipped a small cooler containing detailed instructions, and sampling supplies (gloves, two sets of three 2–mL polypropylene centrifuge tubes, and an ice pack). Instructions directed participants to rinse each tube three times, then fill half full, cap and chill until shipment. Samples were collected one time between July and December 2021 with sampling times varying throughout the day and without precleaning, screen removal or flushing of the sample tap. We requested samples from households without point of entry treatment and from faucets without a point-of-use treatment system (note, 1 location reported treatment after the sample was collected). All samples (three centrifuge tubes per sample) were collected in duplicate, and one set was frozen for archival.

PFAS data from an additional 307 tapwater samples (112 private-wells and 195 public-supply) collected as part of the USGS point-of-use tapwater research effort between 2016 and 2021 were also included herein (Table S1). USGS point-of-use tapwater research is conducted modularly with individual community-based studies (designed to address community priorities and support public-health decisions by individuals, communities, and public-health agencies) informing a national perspective in aggregate. Tapwater sampled in 2016 were collected in three 15-mL Falcon tubes, shipped on ice to the EPA National Exposure Research Laboratory (NERL) and extracted onto a solid phase extraction cartridge (SPE) prior to analysis based on methods described previously (Romanok et al., 2018c; Strynar, 2017; Strynar et al., 2015). Tapwater sampled 2017–2018 were collected in

15-mL Falcon tubes and shipped on ice to the Colorado School of Mines (CSM) laboratory where they were prepared for analysis based on previously published methods (Murray et al., 2019). All tapwater samples collected 2019–2021 were sent to the USGS National Water Quality Laboratory (NWQL) in three 2-mL polypropylene centrifuge tubes that had been rinsed three times prior to sampling, placed in a whirl pack bag and shipped on ice to the laboratory where they were stored frozen prior to analysis (Kolpin et al., 2021; Romanok et al., 2018c). Detailed information on previous study designs, site selection and sample collection are provided elsewhere (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021b; Bradley et al., 2022; Romanok et al., 2018c.

2.2. Analytical methods and quality assurance

Across all studies, PFAS were analyzed by three different laboratories: 1) EPA National Exposure Research Laboratory (NERL, 1 study, 26 samples) in 2016, 2) Colorado School of Mines (CSM, 3 studies, 82 samples) in 2017–2018, and 3) USGS National Water Quality Laboratory (NWQL, 6 studies, 608 samples) in 2019–2021, using previously published methods (Supplemental Information; Tables S1-S2). Potential effects (e.g., bias) associated with the use of different laboratories with varying detection limits and number/types of PFAS analyzed was addressed during statistical analysis.

The EPA NERL (Strynar, 2017; Strynar et al., 2015) method included the analysis of 10 PFAS that were first extracted onto a solid phase extraction (SPE) cartridge, eluted with methanol/ammonia solution and

analyzed by ultra-high performance liquid chromatography (UPLC)-tandem mass spectrometry (MS/MS) operated in negative electrospray ionization (ESI) mode. The CSM method (Murray et al., 2019) included the analysis of 28 and 44 PFAS (Tables S2 and S3) using liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QToF-MS) in negative electrospray ionization (ESI-) mode. The USGS method (Kolpin et al., 2021) included the analysis of 34 total PFAS (including PFOS and PFHxS reported separately as branched and linear) by matrix-modified samples and direct aqueous injection-liquid chromatography/tandem mass spectrometry (DAI-LC/MS/MS) with isotope-dilution quantification. Data were acquired in dynamic multiple reaction monitoring (dMRM) mode with two transitions per analyte for confirmation (except for PFBA and PFPeA that only had one confirming ion).

Method detection limits ranged from 0.1 to 61.8 ng/L depending on compound and laboratory (Table S3). Known bias associated with the variability in laboratory detection limits was accounted for in the selection of statistical models. Quantitative ($\geq$limit of quantitation (LOQ)) and semi-quantitative (between LOQ and long-term method detection limit, LMDL) results were treated as detections. Quality-assurance/quality-control included analyses of field blanks and stable isotope surrogates. The median surrogate recovery for PFAS across all studies and laboratories was 103% (interquartile range (IQR): 93–116%) and the median matrix spike recovery (N = 84) was 107% (IQR: 96–117%). For detailed information on PFAS recoveries by individual and study see Table S1 for links to all available data. Field blanks from the nine individual studies conducted 2016–2021 are detailed in the supporting information section and elsewhere (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2023a; Bradley et al., 2021a; Bradley et al., 2021b; Bradley et al., 2022; Romanok and Bradley, 2021; Romanok and Bradley, 2018; Meppelink et al., 2022; Romanok et al., 2019; Romanok et al., 2018a; Romanok et al., 2018b; Romanok et al., 2023b; Romanok et al., 2023a; Romanok et al., 2022). For the new samples collected by our volunteer network, field blanks were collected by 47 volunteers selected at random from 37 states in 2021. PFBA was the only PFAS detected (one blank sample, 72.3 ng/L), resulting in the censoring of one value (52.1 ng/L) from the associated environmental sample (Romanok et al., 2023c).

2.3. Geospatial analysis

The geospatial analysis joined the 716 sample site locations with numerous geospatial layers and rasters to provide more detailed information regarding each sample site (Seawolf et al., 2023). The datasets included: sources listed in the EPA ECHO (Enforcement and Compliance History Online) Database as potential PFAS environmental release sites including broad categories such as airports, industry, waste management, oil and gas, and department of defense; land-use classes from both the National Land Cover Database (NLCD) and Coastal Change Analysis Program (C-CAP) (Seawolf et al., 2023; Multi-Resolution Land Characteristics Consortium, 2011; National Oceanic and Atmospheric Administration, 2022). A five-km spatial buffer was established around each sample site as a means of capturing the number of PFAS in close proximity to the sampling location and to calculate an average distance to source. Within that buffer each sample site was joined with proximal PFAS sources identified from the EPA ECHO dataset. This join resulted, for many sites included, in multiple potential PFAS sources proximal to each sample site.

We also performed a spatial analysis of the NLCD and C-CAP datasets around each sample site, collecting land use data within the five-km buffer. NLCD data from 2011 was used for both the continental US and Alaska. C-CAP data was available for the Hawaiian Islands. For the island of Hawaii, Maui, and Kuai we used C-CAP data from 2010. For the island of Oahu, C-CAP data from 2011 was used. C-CAP data from 2010 was used for the island of Puerto Rico and for the island of St. Thomas, C-CAP data from 2012 was used. Merging the C-CAP dataset with NLCD was not problematic. We followed the convention outlined in Table S4 to convert C-CAP classes to NLCD classes.

2.4. Statistical analysis

Three different Bayesian hierarchical statistical modeling approaches – employing different distributional assumptions – were used to accommodate the unique aspects of the three primary goals of the analysis. The modeling approaches included (1) a hierarchical regression model to accommodate left-censored observations (observations below detection limits) for individual PFAS (Qian et al., 2004; Wu et al., 2011); (2) a hierarchical Tweedie compound Poisson linear model to model the total PFAS data, which included skewed continuous observations of total PFAS concentrations and many sites with no PFAS detections (i.e., there is zero inflation); and (3) a hierarchical negative binomial regression to model the number of compounds detected at each site. Each of these three modeling approaches are discussed in more detail below and in the Supplemental Information section 1.2.

The Bayesian hierarchical approach to accommodating left-censored data that we employ is robust, and simulation studies have shown it performs well for recovering true contaminant distributions and can handle relatively high proportions of left-censored observations in the dataset (Qian et al., 2004; Stow et al., 2018). For each modeling approach, we fitted two models, a source model that evaluated potential differences between tapwater sources (private or public) and a geospatial model, in which some of the landscape properties hypothesized to influence PFAS concentrations and occurrence were included as predictor variables. For the source model, tapwater source was included as an indicator variable, with public-supply tapwater as the reference cell. For the geospatial models, we included those predictors that were not highly correlated with one another (r < 0.60). The final set of geospatial predictors included the proportion of total developed land, developed open land, cultivated agricultural land, and pasture agricultural land, along with the average distance to the nearest EPA ECHO site. All predictor variables were standardized (mean = 0, standard deviation = 1) prior to analysis. Because land use geospatial variables were highly skewed, they were logit-transformed prior to standardization. For individual PFAS analysis, we limited statistical analysis to those compounds that were measured above their respective detection limits in at least 5% of sites, resulting in inclusion of 8 compounds (PFBA, PFBS, PFHxA, PFHxS, PFOA, PFOS, PFPeA, PFPeS). We chose 5% of the sites as a cutoff because this provided enough observations that were recorded above the detection limit to allow for meaningful inferences of estimated parameters (i.e., lower than 5% resulted in very little information on concentrations above the detection limit to inform parameter estimates). The study, from which data were collected was included as a random effect in all models. All estimated parameters are reported using the posterior mean and 95% credible intervals (CRIs). The code for Bayesian model fitting and posterior inference is available at https://doi.org/10.5066/P9MCYEVS.

2.5. Screening-level assessment

A screening-level assessment (Goumenou and Tsatsakis, 2019; U.S. Environmental Protection Agency, 2011) of potential cumulative biological activity of available individual PFAS in each tapwater sample was conducted using two analogous bioactivity-weighted approaches (Σ_{EAR}, Σ_{TQ}) as described previously (Blackwell et al., 2017; Bradley et al., 2019; Bradley et al., 2018). The EAR approach is a considered a high-level screening of the potential for molecular-scale vertebrate effects to complement the Hazard Index (i.e., TQ) approach. The ToxCast vertebrate-centric *in vitro* effects library was specifically assembled to inform the potential for human biological effects (Blackwell et al., 2017). The ToxEval version 1.3.0 (De Cicco et al., 2018) was used to sum (non-interactive, concentration addition model, e.g., (Altenburger et al., 2018; Cedergreen et al., 2008; Stalter et al., 2020)) individual exposure activity ratios (EAR) from the Toxicity ForeCaster (ToxCast, high-

throughput screening data (U.S. Environmental Protection Agency, 2022c) to estimate sample-specific cumulative EAR ($\sum$EAR) (Blackwell et al., 2017; Bradley et al., 2018). EAR is the ratio of the detected concentration in the sample to the activity concentration at cutoff (ACC) obtained from the ToxCast database. The ACC estimates the point of departure concentration at which a defined threshold of response (cutoff) is achieved for a given biological activity and is less prone to violations of relative potency assumptions (Blackwell et al., 2017). ACC data in the ToxEval v1.3.0 employed in the present study were from the August 2022 invitroDBv3.5 release of the ToxCast database including updated bioactivity information for individual PFAS (U.S. Environmental Protection Agency, 2022c). Non-specific-endpoint, baseline, and unreliable response-curve assays were excluded (Blackwell et al., 2017; Bradley et al., 2018). $\sum$EAR results are summarized in Table S10.

Because the $\sum$EAR approach was limited to 11 individual PFAS in ToxCast, an analogous human-health-based assessment (Goumenou and Tsatsakis, 2019; U.S. Environmental Protection Agency, 2012; U.S. Environmental Protection Agency, 2011) using available federal, state or international human-health benchmarks for 15 individual PFAS was also conducted to sum the toxicity quotient (TQ; ratio of detected concentration to corresponding health–based benchmark) of individual detections to estimate sample-specific cumulative TQ ($\sum$TQ) (Corsi et al., 2019). A precautionary screening–level approach was employed based on the most protective human-health benchmark (i.e., lowest benchmark concentration) available (Interstate Technology Regulatory Council, 2022). $\sum$TQ results and respective health–based benchmarks are summarized in Tables S10 and S5, respectively. Screening assessments were conducted in the program R version 3.6.1 (R Development Core Team, 2019). Differences (centroids and dispersions) among sample types (private-wells and public-supply) for Σ_{EAR} and Σ_{TQ} were assessed by one-way PERMANOVA (n = 9999 permutations) on Euclidean distance (Hammer et al., 2001).

3. Results and discussion

3.1. Spatial and temporal assessments of PFAS exposure in tapwater

In the US and globally, limited information is available on PFAS in point-of-use tapwater, with most drinking-water studies focused on samples from source waters (McMahon et al., 2022; Sims et al., 2022) or pre-distribution samples from community water supplies (Andrews and Naidenko, 2020; Hu et al., 2016; Kurwadkar et al., 2022; Li et al., 2022; McMahon et al., 2022; Neuwald et al., 2022; Post et al., 2013), largely omitting distribution system factors (e.g., plumbing material with PFAS or sorption/degradation in the supply network; (Mohammadi et al., 2022) and a notable paucity of data available for private-wells across the US. To address this gap, we utilized targeted analysis of up to 44 PFAS in point-of-use tapwater from 269 private-wells and 447 public-supply collected 2016–2021 as fractional indicators of the presumptive 8000 + PFAS contaminant (U.S. Environmental Protection Agency, 2022a) (Fig. 1, Figure S1, Table S1). Consistent with other studies and large datasets focused on public–supply tapwater (Hu et al., 2016; Li et al., 2022; McMahon et al., 2022; Post et al., 2013), at least one PFAS was observed in 30% (237 of the 716) of the tapwater samples collected throughout the US (Fig. 1, Figure S2). Based on data from the UCMR3, about 4% of US drinking-water treatment plants tested had detectable PFAS but the breadth of contamination was likely missed due to high detection limits (10–90 ng/L depending on individual PFAS) and a limited number of PFAS analyzed (Hu et al., 2016). More recently, assuming lower detection limits, Andrews and Naidenko (2020) estimated that approximately half the US population likely receive water with PFOA/PFOS concentrations<1 ng/L, but this information has yet to be validated fully with field data particularly at the point-of-use. In our study, seventeen PFAS were detected at least once and, apart from perfluoropropane sulfonic acid (PFPrS), all detected PFAS were analyzed in > 600 samples (Table S2). Reporting limits for the PFAS

observed in the current study varied by laboratory and ranged from 0.1 to 20 ng/L (Table S3). The most frequently detected PFAS analyzed by all laboratories included PFBS (16%), PFHxS (15%), and PFOA (14%), similar to results reported by others for drinking-water resources (surface water intakes or groundwater wells) or community water supplies (Andrews and Naidenko, 2020; Boone et al., 2019; McMahon et al., 2022; Post et al., 2013; Teymoorian et al., 2023). The number of individual PFAS observed ranged from one to nine (median of two) with detected concentrations ranging from 0.025 to 319 ng/L (median: 2.88 ng/L) and corresponding cumulative PFAS concentrations (sum of 16 detected PFAS) ranging from 0.348 to 346 ng/L (median: 7.00 ng/L; Table S10). As expected, sites classified as 'low' impact had the lowest prevalence of PFAS compared to sites near known PFAS sources, whereas PFAS varied widely among sites classified as 'medium.'.

At least one PFAS was detected in 20% of private-well (55/269) and 40% of the public-supply (182/447) samples collected throughout the US. A similar pattern was reported in groundwater from the eastern US, in which 60% of the public-supply wells and 20% of monitoring wells contained at least one PFAS (McMahon et al., 2022). Median cumulative PFAS concentrations (estimated considering detection limits and including study as a random effect) were comparable between public-supply (median = 7.1 ng/L [95% CRI = 2.3, 17.1]) and private–well point-of-use tapwater (median = 8.2 ng/L [95% CRI = 2.6, 20.5]; Fig. 2). Similarly, considering only PFAS with > 5% detections, we observed no differences in estimated median concentrations of individual PFAS or in the number of detected individual PFAS between public-supply and private-well point-of-use tapwater samples (Fig. 2, Tables S7-8). We chose 5% as a cutoff because this provided enough observations above the detection limit to allow for meaningful inferences of estimated parameters. Based on model predictions (Figure S3), the probability of not detecting PFAS above our detection limits ranged from approximately 25% in urban centers (e.g., Chicago) or areas with a known history of PFAS contamination (e.g., Cape Cod (Bradley et al., 2021a)) to > 75% in rural areas (e.g., Northern Plains (Bradley et al., 2022)). Figure S3 illustrates the spatial (among-study) variability that exists in PFAS occurrence (and concentration, not shown) quantified by the study random effect included in all models to account for variability in detection limits and the difference in numbers of PFAS included in each method (Tables S7-8, S10-11). Across all studies, the probability of detecting one PFAS was approximately 18%, with a marked decrease in probability with increasing number of detected compounds; no differences were observed between public-supply and private-well samples (Fig. 3).

Due in large part to funding constraints and prioritization of population-relevant reconnaissance of a range of exposure points within a given community, point-of-use tapwater exposure studies conducted to date (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2023a; Bradley et al., 2021a; Bradley et al., 2021b; Bradley et al., 2023b) typically have employed a one-time spatial–synoptic approach, which provides limited to no insight into point-of-use tapwater temporal variability. To address this data gap, PFAS samples were collected temporally at 3 of the residential locations (2 private-wells, 1 public-supply). The rural, private–well location in South Carolina had no PFAS detected during three months of sampling. PFAS were detected at the suburban public-supply and private-well locations in New Jersey, and cumulative detected concentrations were generally stable (hourly increasing to weekly samples) over 3 months (Figures S4, S5). In light of the near-detection-limit concentrations of several individual PFAS detections, the observed variabilities in detections of some individual PFAS and in per-sample cumulative PFAS detections (Figure S4) were likely due more to method–sensitivity limitations (Teymoorian et al., 2023) than to short-term changes in drinking-water resources. New Jersey (NJ), one of the more proactive states regarding PFAS regulation, has established enforceable NJ-MCLs for three PFAS including PFOA (14 ng/L), PFNA (13 ng/L) and PFOS (13 ng/L) (New Jersey Department of Environmental Protection, 2022a) and has added PFOA, PFOS and PFNA
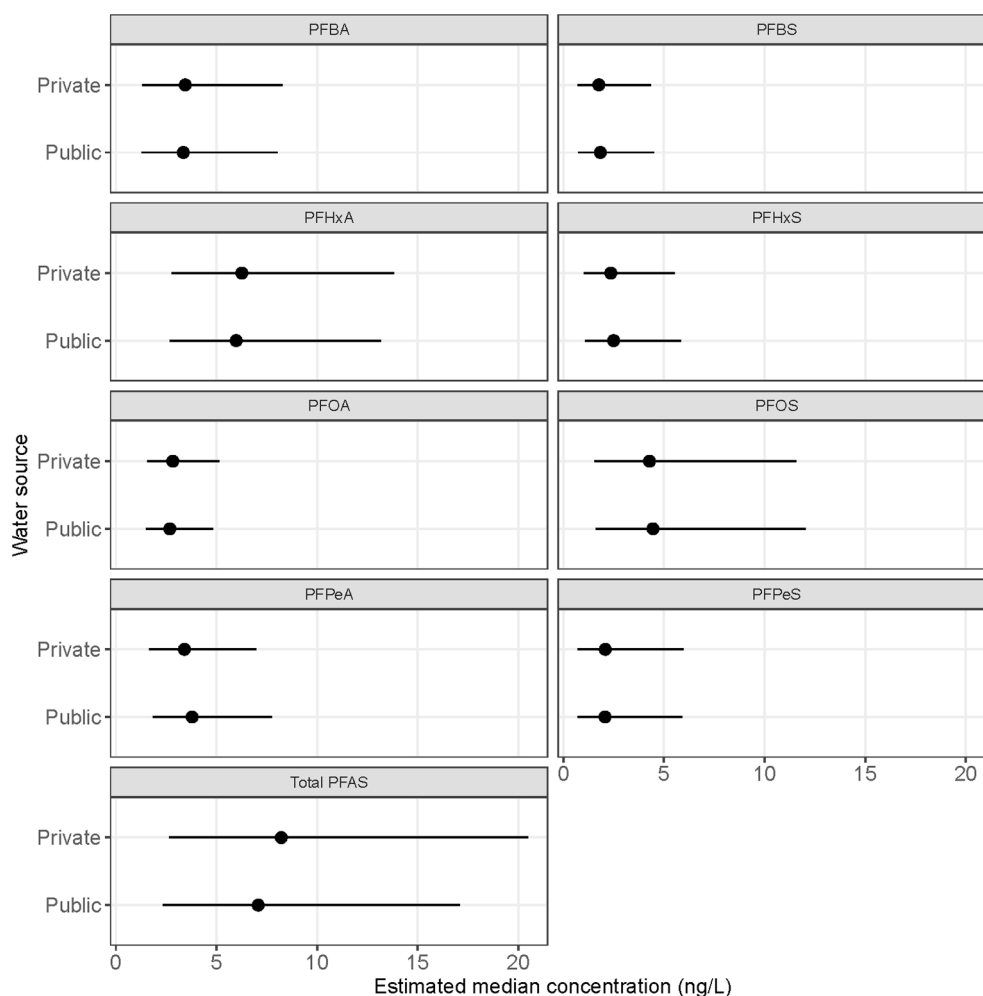
Fig. 2. Estimated median concentrations (ng/L) of select per- and polyfluoroalkyl substances (PFAS) and cumulative PFAS in private-wells and public-supply samples. Circles are posterior means and horizontal lines are 95% credible intervals.

to the Private-well Testing Act, which requires homeowners to test potable wells prior to sale and landlords to test their well water and report results to the tenant once every five years (New Jersey Department of Environmental Protection, 2022b). None of the detections in either location exceeded NJ-MCLs. These results further support the need for continued monitoring of PFAS in point-of-use tapwater from residential private-wells as well as for continued temporal assessments to accurately assess PFAS exposures at the point-of-use more broadly.

3.2. Comparison to proposed US drinking water regulations

Newly proposed MCLs for PFOA (4 ng/L) and PFOS (4 ng/L) were released in March 2023 by EPA as part of the National Primary Drinking-water Standards Rule (U.S. Environmental Protection Agency, 2023b). The proposed MCL for PFOS was below the reporting limit for two of the three laboratories (CSM:1.3 ng/L, NERL: 5.0 ng/L and USGS: 7.4 ng/L; Table S3) used during this study; consequently, our estimates of samples exceeding the proposed MCL should be considered conservative. The reporting limit for PFOA was above the proposed MCL for only one laboratory (CSM: 1.3 ng/L, NERL: 5 ng/L, USGS: 2.0 ng/L; Table S3) in which the least number of samples were analyzed (26/716; Table S1). Proposed MCLs for PFOA and PFOS were exceeded in 6.7% and 4.2%, respectively, of all tapwater samples collected but were exceeded in 48% (48 of 99) and 70% (30 of 43), respectively, of tapwater samples when detected. Further, proposed MCLs for PFOA and PFOS were exceeded in 63% and 67%, respectively of the private-well tapwater samples and in

44% and 77%, respectively of the public-supply tapwater samples, when detected. The proposed MCLG (zero) (U.S. Environmental Protection Agency, 2023b) was de facto exceeded in every sample in which PFOS and PFOA was detected (private-well: 15 and 24, respectively; public-supply: 28 and 75, respectively). Further, to account for dose additive noncancer effects of PFBS, PFNA, PFHxS, GenX, EPA proposed an MCL for the mixture of these four PFAS based on a hazard index approach (U.S. Environmental Protection Agency, 2020). The proposed hazard index of 1 for the sum of the toxicity quotient (measured concentration/health-based value) for PFBS + PFNA + PFHxS + GenX was exceeded in 4.6% of tapwater collected.

3.3. Aggregated screening-level assessments

We also used two bioactivity weighted screening approaches Σ_{EAR} and Σ_{TQ} to provide insight into the potential aggregated (sum of all PFAS) effects. These approaches are limited by the availability of weighting factors (ToxCast ACC and health-based benchmarks, respectively) and mixture effects are estimated by assuming concentration addition (Cedergreen, 2014). The Σ_{EAR} approach has been used effectively in other studies as a protective (conservative) screening tool to asses drinking-water exposure risk to organic contaminant mixtures because it leverages response relations for>9000 organic chemicals across over 1000 standardized vertebrate cell lines (Kavlock et al., 2012; Kavlock et al., 2008; Richard et al., 2016). Contaminant bioactivity ratios were aggregated across all ToxCast endpoints available for
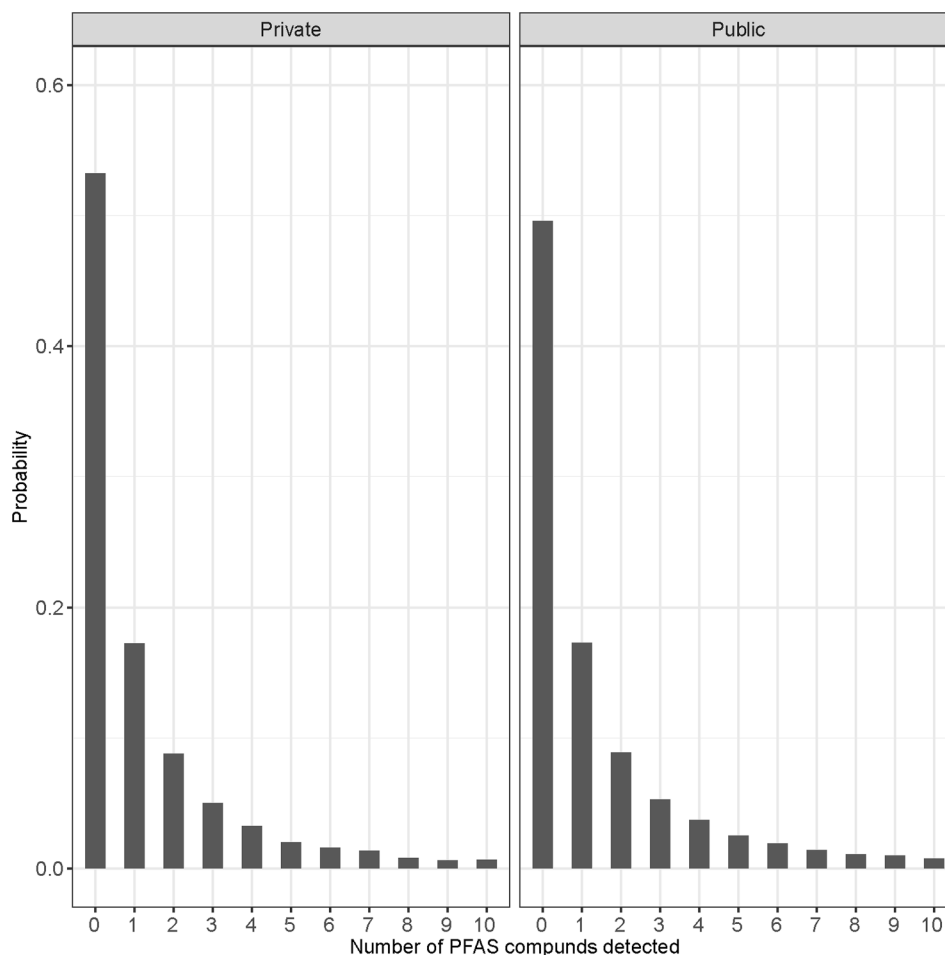
Fig. 3. The predicted posterior probability of detecting 1 – 10 per- and polyfluoroalkyl substances (PFAS) in private-well and public water-supply tapwater.

individual PFAS without restriction to recognized modes of action to provide a precautionary lower-bound estimate of in vivo adverse-effect levels (Paul Friedman et al., 2020), however, this approach may not accurately reflect apical effects (Blackwell et al., 2017; Schroeder et al., 2016). Further, for PFAS, the approach has the potential to underestimate exposure risk because only 11 of the detected compounds had exact Chemical Abstract Services number matches in the ToxCast™ database and only six (PFOS, PFOA, PFNA, PFHpA, PFBA, PFHxS) of these had EAR exceeding our lowest threshold for consideration (>0.00001). The $\sum_{TQ}$ approach targets apical human-health effects, is notably constrained to recognized (i.e., benchmarked) health concerns and was used herein to estimate cumulative effects from a broader suite of PFAS (15 with established health-based benchmarks; Table S5) (Interstate Technology Regulatory Council, 2022). Lastly, it is important to note, the EAR approach is based on measured endpoint-specific activity cutoff concentrations, whereas the human-health benchmarks used in the TQ approach generally include a margin of safety (margin of exposure).

None of the samples exceeded a $\Sigma_{EAR} > 1$, a value which indicates cumulative exposure at concentrations capable of modulating molecular endpoints *in vitro,* and we observed no systematic differences in Σ_{EAR} between private–well and public–supply locations (Fig. 4). However, 65 tapwater samples exceeded the $\Sigma_{EAR} = 0.001$ precautionary screening level of potential concern (yellow line, Fig. 4; Table S10) for molecular effects described previously (Bradley et al., 2018). For PFAS and PFOA, which proposed MCLGs of zero, EPA's interim health advisory levels released in 2022 (U.S. Environmental Protection Agency, 2022a) were used as the benchmark value (Table S5). Σ_{TQ} values were higher in private–well tapwater samples compared to public–supply (p = 0.0015),

and 124 samples overall had $\Sigma_{TQ} > 1$ (Fig. 4, Table S10), indicating a high probability of aggregated risk when considering exposures to all observed PFAS with an available benchmark. As expected, given their proposed MCLG of zero (U.S. Environmental Protection Agency, 2023b), Σ_{TQ} results were driven by PFOA and PFOS, when detected. Simultaneous detection of multiple PFAS is consistent with other drinking-water (Andrews and Naidenko, 2020; Boone et al., 2019; Hu et al., 2016) and tapwater studies (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021b) in the US. The results of precautionary Σ_{EAR} and Σ_{TQ} assessments by this group indicate that the potential for human-health effects from contaminant exposures (including PFAS) through drinking-water are common and comparable in private-well and public-supply tapwater (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021a). Information generated by this study and elsewhere indicates the need for further assessments of cumulative health exposure risks of PFAS mixtures (Kwiatkowski et al., 2020) and of PFAS in combination with other organic and inorganic contaminants of concern, particularly in unmonitored/unregulated private-wells where information is limited or not available.

3.4. Predicting exposure based on potential sources and land-use

The final model comparing tapwater PFAS concentrations to geospatial drivers included median distance to potential source (including airport, industry, waste management, oil and gas, and department of defense) and several land-use classifications (total developed, open developed, cultivated and pasture agriculture). The number of PFAS sources in a 5–km buffer around each site was highly correlated with developed land-use (r = 0.66) and was excluded from the model.
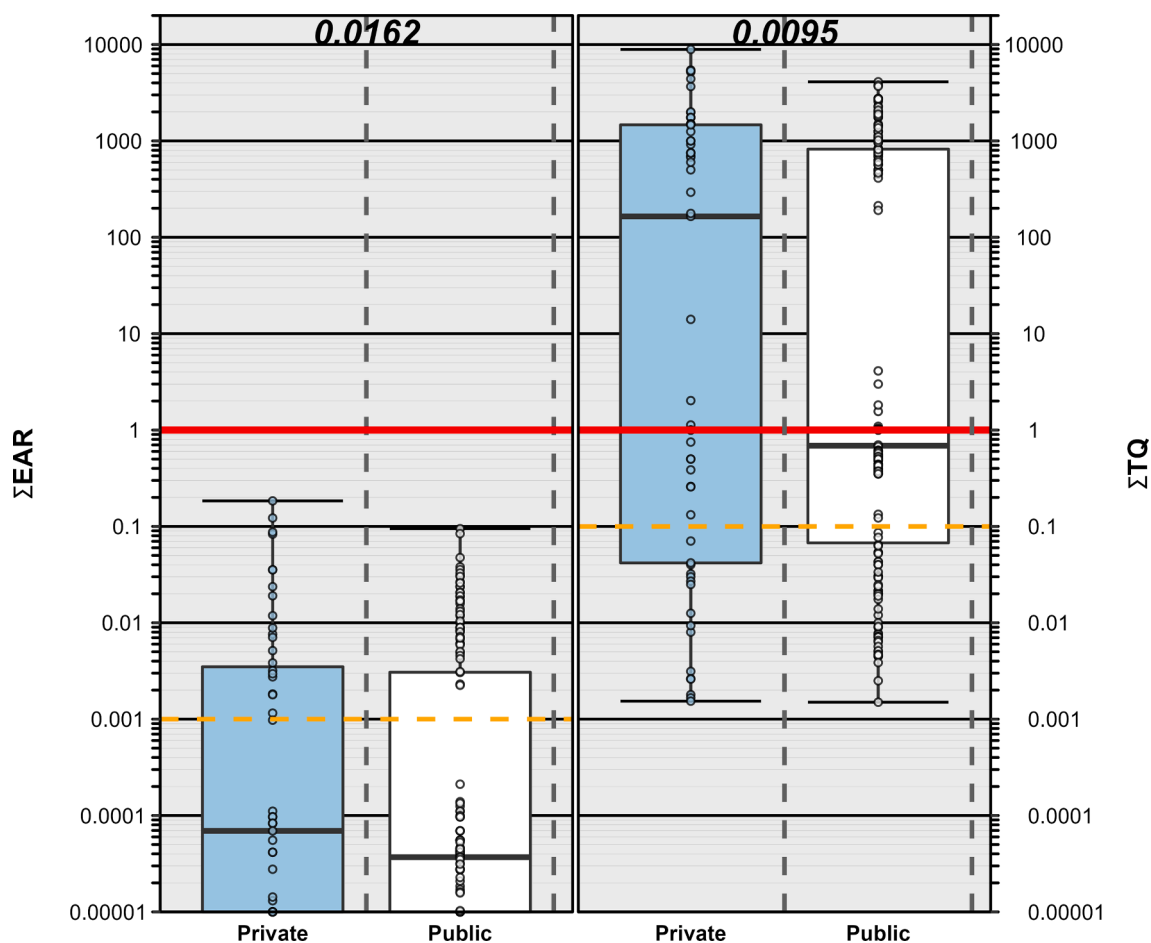
Fig. 4. Left. Cumulative maximum Exposure-Activity Ratios ($\sum$EAR) across all assays for 9 individual per- and polyfluoroalkyl substances (PFAS) in ToxCast and detected in tapwater collected from public-supply and private-wells. Solid red and yellow lines indicate concentrations shown to modulate effects *in vitro* and effects-screening-level thresholds (EAR = 1 and EAR = 0.001), respectively. Right. Human-health benchmark cumulative toxicity quotient (ΣTQ) for 15 PFAS listed in Table S5 and tapwater from public-supply and private-wells. Solid red and yellow lines indicate benchmark equivalent concentrations and effects-screening-level threshold of concern (TQ = 0.1), respectively. Boxes, centerlines, and whiskers indicate interquartile range, median, and 5th and 95th percentiles, respectively. Numbers above each boxplot pair indicate the permuted probability that the centroids and dispersions are the same (PERMANOVA; 9999 permutations). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Cumulative PFAS concentrations and the number of detected compounds increased with surrounding developed–land and decreased with increasing distance from probable source(s) (Fig. 5, Figure S6, Tables S10-11). However, for individual PFAS the distance to probable source(s) was not a strong predictor of concentration (Figure S7, Table S8). PFBS was the only PFAS which exhibited a positive relation with development and pasture agriculture and a negative relation with open development (commonly includes large-lot single-family housing units, parks, golf courses, and vegetation planted in developed settings for recreation, erosion control, or aesthetic purposes). Although bio-solids application is a recognized source of PFAS to surface- and groundwaters in agricultural landscapes (Munoz et al., 2022; Sepulvado et al., 2011), in this study concentrations of PFBS, PFHxA, PFHxS, PFOA and PFOS decreased with increasing surrounding cultivated cropland. Further, for several compounds (PFBA, PFHxA, PFHxS and PFOA), concentrations decreased with increasing development, an unexpected result which suggests that point-of-use tapwater exposure to individual PFAS in our study is more closely associated with the type of PFAS sources (e.g., industry, airport, wastewater, etc., which are generally located at the edge of urban development and not in the highest residentially-developed areas) (Hu et al., 2016) rather than numbers of potential PFAS sources (Salvatore et al., 2022). Because our geospatial analysis was constrained to broad putative-source categories (e.g., military fire training areas, industrial, wastewater) and 90% of the

corresponding potential sources were characterized as industrial, exploration of source-type/point-of-use tapwater exposure relationships was limited and merits further investigation. Further, most public-supply samples were collected at the tap not the treatment facility, indicating a distinct disconnect from PFAS source and drinking water resource. Despite these limitations, the real–world point-of-use tapwater PFAS concentration data compiled herein along a national gradient of presumptive contamination represents an important validation dataset to assess and tune putative-source PFAS contamination models, like that presented recently (Salvatore et al., 2022).

3.5. Implications and future directions

Approximately 40 million people in the US rely on private-wells for drinking-water (DeSimone et al., 2015; Dieter et al., 2018), most national testing programs, like the UCMR3 focused on community water supplies serving $\geq$ 10,000 consumers, do not include private-wells and rarely capture information from rural communities (52 million people rely on small water supplies serving < 10,000), indicating data on PFAS exposure and potential human-health effects is does not exist for over one-third of the US population (Hu et al., 2016). As noted previously, small public supplies and private-wells may be disproportionally affected by PFAS, emphasizing the value of studies like these focused broadly on point-of-use tapwater PFAS exposures, with an emphasis on
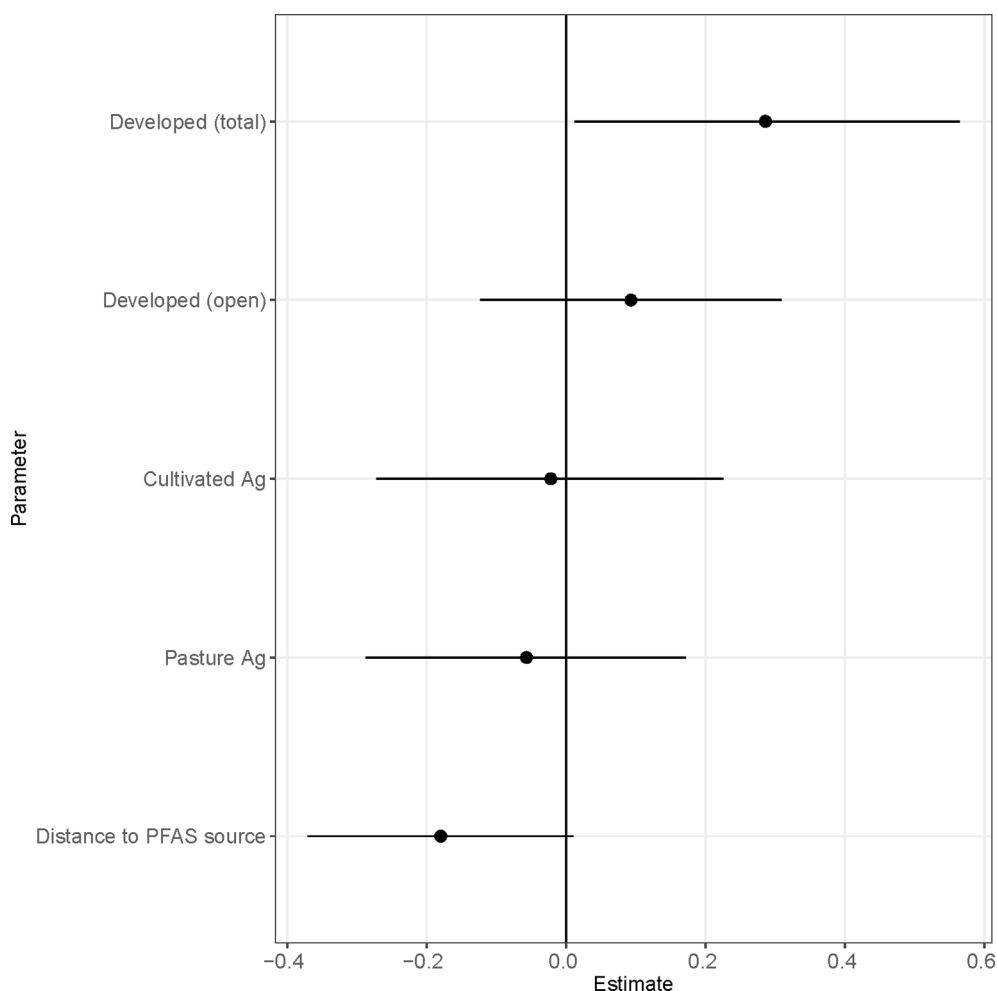
Fig. 5. Estimated effects of geospatial predictor variables on cumulative per- and polyfluoroalkyl substances (PFAS) concentrations. Circles are posterior means and horizontal lines are 95% credible intervals. Geospatial predictors with 95% credible intervals that overlap with zero are not considered statistically significant.

comparing exposures in private-wells with those directly from public-supply using similar sampling/analytical methods. Some of these gaps associated with PFAS in small community public supply facilities may be addressed by the UCMR5, currently underway in the US and expected to provide extensive information on PFAS in US drinking water for public-supply consumers in the next few years (U.S. Environmental Protection Agency, 2023a).

Modeled results indicate that on average at least one PFAS is detected in about 45% of US drinking-water samples. Results also indicate that 1) detection probabilities vary spatially (8% in rural areas up to > 70% in urban areas/areas with a known history of PFAS contamination), 2) drinking-water exposures may be more common in the Great Plains, Great Lakes, Eastern Seaboard, and Central/Southern California regions, and 3) temporal variations in concentrations/detections may be limited. Geospatial datasets and land-use information were correlated with both cumulative PFAS concentrations, and the number of PFAS detected; however, they were not often correlated with specific PFAS profiles due to the limited number of individual PFAS detected more than once using targeted approaches. Targeted PFAS analytes are only a fractional indicator of the 8000 + potential PFAS and the fraction of total organic fluorine captured by these targeted analyses is typically low in surface water (D'Agostino and Mabury, 2017; McDonough et al., 2019) and drinking-water (Jiao et al., 2022). Potential detection of one or more PFAS in US drinking-water combined with the paucity of information available on current use/ultra-short chain compounds (Neuwald et al., 2022) supports the continued need for point-of-use tapwater monitoring, with an emphasis on unmonitored

private-wells and underserved communities on small community water supplies. To fully understand exposure and adequately determine risk to human-health, continued emphasis should be placed on 1) integrating geospatial datasets with PFAS data broadly to identify vulnerable regions/subpopulations, 2) expanding monitoring to include rural small-–system and private–well dependent communities, and 3) expanding target and non-target analysis methods particularly in drinking-water monitoring programs in the US and globally.

CRediT authorship contribution statement

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

All data are available. All data presented can be found in a series of USGS data releases (Meppelink et al., 2022; Romanok and Bradley, 2018; Romanok and Bradley, 2021; Romanok et al., 2022; Romanok et al., 2019; Romanok et al., 2023a; Romanok et al., 2023b; Romanok et al., 2023c). For links to the individual USGS data releases see Table S1.

Acknowledgements

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.108033.

References

Altenburger, R., Scholze, M., Busch, W., Escher, B.I., Jakobs, G., Krauss, M., Krüger, J., Neale, P.A., Ait-Aissa, S., Almeida, A.C., Seiler, T.-B., Brion, F., Hilscherová, K., Hollert, H., Novák, J., Schlichting, R., Serra, H., Shao, Y., Tindall, A., Tollefsen, K.E., Umbuzeiro, G., Williams, T.D., Kortenkamp, A., 2018. Mixture effects in samples of multiple contaminants – an inter-laboratory study with manifold bioassays. Environ. Int. 114, 95–106.

American Academy of Pediatrics, 2009. Policy statement: drinking water from private wells and risks to children. Pediatrics 123, 1599–1605. https://doi.org/10.1542/peds.2009-0751.

Andrews, D.Q., Naidenko, O.V., 2020. Population-wide exposure to per- and polyfluoroalkyl substances from drinking water in the United States. Environ. Sci. Technol. Lett. 7, 931–936. https://doi.org/10.1021/acs.estlett.0c00713.

Bach, C.C., Vested, A., Jørgensen, K.T., Bonde, J.P.E., Henriksen, T.B., Toft, G., 2016. Perfluoroalkyl and polyfluoroalkyl substances and measures of human fertility: a systematic review. Crit. Rev. Toxicol. 46, 735–755. https://doi.org/10.1080/10408444.2016.1182117.

Bao, Y., Deng, S., Jiang, X., Qu, Y., He, Y., Liu, L., Chai, Q., Mumtaz, M., Huang, J., Cagnetta, G., Yu, G., 2018. Degradation of PFOA substitute: GenX (HFPO–DA ammonium salt): oxidation with UV/persulfate or reduction with UV/sulfite? Environ. Sci. Tech. https://doi.org/10.1021/acs.est.8b02172.

Barry, V., Winquist, A., Steenland, K., 2013. Perfluorooctanoic acid (PFOA) exposures and incident cancers among adults living near a chemical plant. Environ. Health Perspect. 121, 1313–1318. https://doi.org/10.1289/ehp.1306615.

Blackwell, B.R., Ankley, G.T., Corsi, S.R., DeCicco, L.A., Houck, K.A., Judson, R.S., Li, S., Martin, M.T., Murphy, E., Schroeder, A.L., Smith, E.R., Swintek, J., Villeneuve, D.L., 2017. An" EAR" on environmental surveillance and monitoring: A case study on the use of exposure-activity ratios (EARs) to prioritize sites, chemicals, and bioactivities of concern in Great Lakes waters. Environ. Sci. Tech. 51 (15), 8713–8724.

Blake, B.E., Fenton, S.E., 2020. Early life exposure to per- and polyfluoroalkyl substances (PFAS) and latent health outcomes: a review including the placenta as a target tissue and possible driver of peri- and postnatal effects. Toxicology 443, 152565. https://doi.org/10.1016/j.tox.2020.152565.

Boone, J.S., Vigo, C., Boone, T., Byrne, C., Ferrario, J., Benson, R., Donohue, J., Simmons, J., Kolpin, D.W., Furlong, E.T., Glassmeyer, S.T., 2019. Per- and polyfluoroalkyl substances in source and treated drinking waters of the United States. Sci. Total Environ. 653, 359–369.

Bradley, P.M., Kolpin, D.W., Romanok, K.M., Smalling, K.L., Focazio, M.J., Brown, J.B., et al., 2018. Reconnaissance of Mixed Organic and Inorganic Chemicals in Private and Public Supply Tapwaters at Selected Residential and Workplace Sites in the United States. Environ. Sci. Tech. 52, 13972–13985. https://doi.org/10.1021/acs.est.8b04622.

Bradley, P.M., Journey, C.A., Berninger, J.P., Button, D.T., Clark, J.M., Corsi, S.R., DeCicco, L.A., Hopkins, K.G., Huffman, B.J., Nakagaki, N., Norman, J.E., Nowell, L. H., Qi, S.L., VanMetre, P.C., Waite, I.R., 2019. Mixed-chemical exposure and predicted effects potential in wadeable southeastern USA streams. Sci. Total Environ. 655, 70–83.

Bradley, P.M., Argos, M., Kolpin, D.W., Meppelink, S.M., Romanok, K.M., Smalling, K.L., Focazio, M.J., Allen, J.M., Dietze, J.E., Devito, M.J., Donovan, A.R., Evans, N., Givens, C.E., Gray, J.L., Higgins, C.P., Hladik, M.L., Iwanowicz, L.R., Journey, C.A., Lane, R.F., Laughrey, Z.R., Loftin, K.A., McCleskey, R.B., McDonough, C.A., Medlock-Kakaley, E., Meyer, M.T., Putz, A.R., Richardson, S.D., Stark, A.E., Weis, C. P., Wilson, V.S., Zehraoui, A., 2020. Mixed organic and inorganic tapwater exposures and potential effects in greater Chicago area, USA. Sci. Total Environ. 719, 137236. https://doi.org/10.1016/j.scitotenv.2020.137236.

Bradley, P.M., LeBlanc, D.R., Romanok, K.M., Smalling, K.L., Focazio, M.J., Cardon, M. C., Clark, J.M., Conley, J.M., Evans, N., Givens, C.E., Gray, J.L., Earl Gray, L., Hartig, P.C., Higgins, C.P., Hladik, M.L., Iwanowicz, L.R., Loftin, K.A., Blaine McCleskey, R., McDonough, C.A., Medlock-Kakaley, R., Weis, C.P., Wilson, V.S., 2021a. Public and private tapwater: Comparative analysis of contaminant exposure and potential risk, Cape Cod, Massachusetts, USA. Environ. Int. 152, 106487. https://doi.org/10.1016/j.envint.2021.106487.

Bradley, P.M., Padilla, I.Y., Romanok, K.M., Smalling, K.L., Focazio, M.J., Breitmeyer, S. E., Cardon, M.C., Conley, J.M., Evans, N., Givens, C.E., Gray, J.L., Gray, L.E., Hartig, P.C., Higgins, C.P., Hladik, M.L., Iwanowicz, L.R., Lane, R.F., Loftin, K.A., McCleskey, R.B., McDonough, C.A., Medlock-Kakaley, E., Meppelink, S., Weis, C.P., Wilson, V.S., 2021b. Pilot-scale expanded assessment of inorganic and organic tapwater exposures and predicted effects in Puerto Rico, USA. Sci. Total Environ. 788, 147721. https://doi.org/10.1016/j.scitotenv.2021.147721.

Bradley, P.M., Romanok, K.M., Smalling, K.L., Focazio, M.J., Charbonneau, R., George, C. M., Navas-Acien, A., O'Leary, M., Red Cloud, R., Zacher, T., Breitmeyer, S.E., Cardon, M.C., Cuny, C.K., Ducheneaux, G., Enright, K., Evans, N., Gray, J.L., Harvey, D.E., Hladik, M.L., Kanagy, L.K., Loftin, K.A., McCleskey, R.B., Medlock-Kakaley, E.K., Meppelink, S.M., Valder, J.F., Weis, C.P., 2022. Tapwater exposures, effects potential, and residential risk management in northern plains nations. Environ. Sci. Technol. Water 2 (10), 1772–1788.

Bradley, P.M., Kolpin, D.W., Thompson, D.A., Romanok, K.M., Smalling, K.L., Breitmeyer, S.E., Cardon, M.C., Cwiertny, D.M., Evans, N., Field, R.W., Focazio, M.J., Beane Freeman, L., Givens, C.E., Gray, J.L., Hager, G.L., Hladik, M.L., Hofmann, J. N., Jones, R.R., Kanagy, L.K., Lane, R.F., McCleskey, R.B., Medgyesi, D., Medlock-Kakaley, E.K., Meppelink, S.M., Meyer, M.T., Stavreva, D.A., Ward, M.H., 2023a. Juxtaposition of intensive agriculture, vulnerable aquifers, and mixed chemical/microbial exposures in private-well tapwater in northeast Iowa. Sci. Total Environ. 868, 161672. https://doi.org/10.1016/j.scitotenv.2023.161672.

Bradley, P.M., Romanok, K.M., Smalling, K.L., Focazio, M.J., Evans, N., Fitzpatrick, S.C., Givens, C.E., Gordon, S.E., Gray, J.L., Green, E.M., Griffin, D.W., Hladik, M.L., Kanagy, L.K., Lisle, J.T., Loftin, K.A., Blaine McCleskey, R., Medlock–Kakaley, E.K., Navas-Acien, A., Roth, D.A., South, P., Weis, C.P., 2023b. Bottled water contaminant exposures and potential human effects. Environ. Int. 171, 107701. https://doi.org/10.1016/j.envint.2022.107701.

Butenhoff, J.L., Chang, S.-C., Ehresman, D.J., York, R.G., 2009. Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. Reprod. Toxicol. 27, 331–341. https://doi.org/10.1016/j.reprotox.2009.01.004.

Cedergreen, N., 2014. Quantifying synergy: a systematic review of mixture toxicity studies within environmental toxicology. PLoS One 9 (5), e96580. https://doi.org/10.1371/journal.pone.0096580.

Cedergreen, N., Christensen, A.M., Kamper, A., Kudsk, P., Mathiassen, S.K., Streibig, J.C., Sørensen, H., 2008. A review of independent action compared to concentration addition as reference models for mixtures of compounds with different molecular target sites. Environ. Toxicol. Chem. 27 (7), 1621. https://doi.org/10.1897/07-474.1.

Charrois, J.W.A., 2010. Private drinking water supplies: challenges for public health. Can. Med. Assoc. J. 182, 1061–1064. https://doi.org/10.1503/cmaj.090956.

Chen, R., Li, G., Yu, Y., Ma, X.u., Zhuang, Y., Tao, H., Shi, B., 2019. Occurrence and transport behaviors of perfluoroalkyl acids in drinking water distribution systems. Sci. Total Environ. 697, 134162. https://doi.org/10.1016/j.scitotenv.2019.134162.

Corsi, S.R., De Cicco, L.A., Villeneuve, D.L., Blackwell, B.R., Fay, K.A., Ankley, G.T., Baldwin, A.K., 2019. Prioritizing chemicals of ecological concern in Great Lakes tributaries using high-throughput screening data and adverse outcome pathways. Sci. Total Environ. 686, 995–1009.

D'Agostino, L.A., Mabury, S.A., 2017. Certain perfluoroalkyl and polyfluoroalkyl substances associated with aqueous film forming foam are widespread in canadian surface waters. Environ. Sci. Tech. 51, 13603–13613. https://doi.org/10.1021/acs.est.7b03994.

De Cicco, L., Corsi, S.R., Villeneuve, D., Blackwell, B.R., Ankley, G.T., 2018. toxEval: Evaluation of measured concentration data using the ToxCast high-throughput screening database or a user-defined set of concentration benchmarks. R package version 1.0.0. 2018; https://rconnect.usgs.gov/toxEval_docs/.

DeSimone, L.A., McMahon, P.B., Rosen, M.R., 2015. The quality of our Nation's waters: water quality in Principal Aquifers of the United States, 1991-2010. 2015; U. S. Geological Survey Circular 1360:161 10.3133/cir1360.

Dieter, C.A., Maupin, M.A., Caldwell, R.R., Harris, M.A., Ivahnenko, T.I., Lovelace, J.K., et al., 2018. Estimated use of water in the United States in 2015. U. S. Geological Survey Circular 1441, 76. https://doi.org/10.3133/cir1441.

Domingo, J.L., Nadal, M., 2019. Human exposure to per- and polyfluoroalkyl substances (PFAS) through drinking water: a review of the recent scientific literature. Environ. Res. 177, 108648. https://doi.org/10.1016/j.envres.2019.108648.

Evich, M.G., Davis, M.J.B., McCord, J.P., Acrey, B., Awkerman, J.A., Knappe, D.R.U., Lindstrom, A.B., Speth, T.F., Tebes-Stevens, C., Strynar, M.J., Wang, Z., Weber, E.J., Henderson, W.M., Washington, J.W., 2022. Per- and polyfluoroalkyl substances in the environment. Science 375 (6580). https://doi.org/10.1126/science.abg9065.

Focazio, M.J., Tipton, D., Dunkle, S.S., Geiger, L.H., 2006. The chemical quality of self-supplied domestic well water in the United States. Ground Water Monit. Rem. 26, 92–104. https://doi.org/10.1111/j.1745-6592.2006.00089.x.

Glüge, J., Scheringer, M., Cousins, I.T., DeWitt, J.C., Goldenman, G., Herzke, D., Lohmann, R., Ng, C.A., Trier, X., Wang, Z., 2020. An overview of the uses of per- and polyfluoroalkyl substances (PFAS). Environ. Sci. Processes Impacts 22 (12), 2345–2373.

Goumenou, M, Tsatsakis, A., 2019. Proposing new approaches for the risk characterisation of single chemicals and chemical mixtures: The source related Hazard Quotient (HQS) and Hazard Index (HIS) and the adversity specific Hazard Index (HIA). Toxicol. Rep. 6, 632–636. https://doi.org/10.1016/j.toxrep.2019.06.010.

Grandjean, P., Budtz-Jørgensen, E., 2013. Immunotoxicity of perfluorinated alkylates: calculation of benchmark doses based on serum concentrations in children. Environ. Health 12, 35. https://doi.org/10.1186/1476-069X-12-35.

Hammer, Ø., Harper, D.A., Ryan, P.D., 2001. PAST: paleontological statistics software package for education and data analysis. Palaeontol. Electron. 4, 9. https://palaeo-el ectronica.org/2001_1/past/issue1_01.htm.

Houtz, E.F., Higgins, C.P., Field, J.A., Sedlak, D.L., 2013. Persistence of perfluoroalkyl acid precursors in AFFF-impacted groundwater and soil. Environ. Sci. Tech. 47, 8187–8195. https://doi.org/10.1021/es4018877.

Hu, X.C., Andrews, D.Q., Lindstrom, A.B., Bruton, T.A., Schaider, L.A., Grandjean, P., Lohmann, R., Carignan, C.C., Blum, A., Balan, S.A., Higgins, C.P., Sunderland, E.M., 2016. Detection of poly- and perfluoroalkyl substances (PFASs) in U.S. drinking water linked to industrial sites, military fire training areas, and wastewater treatment plants. Environ. Sci. Technol. Lett. 3 (10), 344–350.

Hu, X.C., Tokranov, A.K., Liddie, J., Zhang, X., Grandjean, P., Hart, J.E., Laden, F., Sun, Q.i., Yeung, L.W.Y., Sunderland, E.M., 2019. Tap water contributions to plasma concentrations of poly- and perfluoroalkyl substances (PFAS) in a nationwide prospective cohort of U.S. Women. Environmental Health Perspectives 127 (6), 067006. https://doi.org/10.1289/ehp4093.

Interstate Technology Regulatory Council, 2022. PFAS — Per- and Polyfluoroalkyl Substances. 2022; https://pfas-1.itrcweb.org/.

Jiao, E., Zhu, Z., Yin, D., Qiu, Y., Kärrman, A., Yeung, L.W.Y., 2022. A pilot study on extractable organofluorine and per- and polyfluoroalkyl substances (PFAS) in water from drinking water treatment plants around Taihu Lake, China: what is missed by target PFAS analysis? Environ. Sci. Processes Impacts 24, 1060–1070. https://doi.org/10.1039/d2em00073c.

Kavlock, R.J., Ankley, G., Blancato, J., Breen, M., Conolly, R., Dix, D., Houck, K., Hubal, E., Judson, R., Rabinowitz, J., Richard, A., Setzer, R.W., Shah, I., Villeneuve, D., Weber, E., 2008. Computational toxicology—a state of the science mini review. Toxicol. Sci. 103 (1), 14–27.

Kavlock, R., Chandler, K., Houck, K., Hunter, S., Judson, R., Kleinstreuer, N., Knudsen, T., Martin, M., Padilla, S., Reif, D., Richard, A., Rotroff, D., Sipes, N., Dix, D., 2012. Update on EPA's ToxCast program: providing high throughput decision support tools for chemical risk management. Chem. Res. Toxicol. 25 (7), 1287–1302. https://doi.org/10.1021/tx3000939.

Kolpin, D.W., Hubbard, L.E., Cwiertny, D.M., Meppelink, S.M., Thompson, D.A., Gray, J. L., 2021. A comprehensive statewide spatiotemporal assessment of per- and polyfluoroalkyl substances (PFAS) in an agricultural region of the United States. Environ. Sci. Technol. Lett. 8, 981–988. https://doi.org/10.1021/acs.estlett.1c00750.

Kurwadkar, S., Dane, J., Kanel, S.R., Nadagouda, M.N., Cawdrey, R.W., Ambade, B., Struckhoff, G.C., Wilkin, R., 2022. Per- and polyfluoroalkyl substances in water and wastewater: a critical review of their global occurrence and distribution. Sci. Total Environ. 809, 151003. https://doi.org/10.1016/j.scitotenv.2021.151003.

Kwiatkowski, C.F., Andrews, D.Q., Birnbaum, L.S., Bruton, T.A., DeWitt, J.C., Knappe, D. R.U., Maffini, M.V., Miller, M.F., Pelch, K.E., Reade, A., Soehl, A., Trier, X., Venier, M., Wagner, C.C., Wang, Z., Blum, A., 2020. Scientific basis for managing PFAS as a chemical class. Environ. Sci. Technol. Lett. 7 (8), 532–543.

Li, X., Fatowe, M., Cui, D., Quinete, N., 2022. Assessment of per- and polyfluoroalkyl substances in Biscayne Bay surface waters and tap waters from South Florida. Sci. Total Environ. 806, 150393. https://doi.org/10.1016/j.scitotenv.2021.150393.

Li, J., He, J., Niu, Z., Zhang, Y., 2020. Legacy per- and polyfluoroalkyl substances (PFASs) and alternatives (short-chain analogues, F-53B, GenX and FC-98) in residential soils of China: Present implications of replacing legacy PFASs. Environ. Int. 135, 105419. https://doi.org/10.1016/j.envint.2019.105419.

Liu, G., Dhana, K., Furtado, J.D., Rood, J., Zong, G., Liang, L., Qi, L.u., Bray, G.A., DeJonge, L., Coull, B., Grandjean, P., Sun, Q.i., Basu, S., 2018. Perfluoroalkyl substances and changes in body weight and resting metabolic rate in response to weight-loss diets: a prospective study. PLoS Med. 15 (2), e1002502. https://doi.org/10.1371/journal.pmed.1002502.

Masoner, J.R., Kolpin, D.W., Cozzarelli, I.M., Barber, L.B., Burden, D.S., Foreman, W.T., Forshay, K.J., Furlong, E.T., Groves, J.F., Hladik, M.L., Hopton, M.E., Jaeschke, J.B., Keefe, S.H., Krabbenhoft, D.P., Lowrance, R., Romanok, K.M., Rus, D.L., Selbig, W. R., Williams, B.H., Bradley, P.M., 2019. Urban stormwater: an overlooked pathway of extensive mixed contaminants to surface and groundwaters in the United States. Environ. Sci. Tech. 53 (17), 10070–10081.

Masoner, J.R., Kolpin, D.W., Cozzarelli, I.M., Smalling, K.L., Bolyard, S.C., Field, J.A., Furlong, E.T., Gray, J.L., Lozinski, D., Reinhart, D., Rodowa, A., Bradley, P.M., 2020. Landfill leachate contributes per-/poly-fluoroalkyl substances (PFAS) and pharmaceuticals to municipal wastewater. Environ. Sci. Water Res. Technol. 6 (5), 1300–1311.

McDonough, C.A., Guelfo, J.L., Higgins, C.P., 2019. Measuring total PFASs in water: the tradeoff between selectivity and inclusivity. Curr. Opin. Environ. Sci. Health 7, 13–18. https://doi.org/10.1016/j.coesh.2018.08.005.

McMahon, P.B., Tokranov, A.K., Bexfield, L.M., Lindsey, B.D., Johnson, T.D., Lombard, M.A., Watson, E., 2022. Perfluoroalkyl and polyfluoroalkyl substances in groundwater used as a source of drinking water in the eastern United States. Environ. Sci. Tech. 56 (4), 2279–2288.

Meppelink, S.M., Bradley, P.M., Romanok, K.M., Kolpin, D.W., 2022. Target-chemical concentrations, exposure activity ratios, and bioassay results for assessment of mixed-organic/inorganic chemical exposures in northeast Iowa private-well tapwater, 2018-19. 2022; U.S. Geological Survey data release. 10.5066/P9IYT37H.

Mohammadi, A., Dobaradaran, S., Schmidt, T.C., Malakootian, M., Spitz, J., 2022. Emerging contaminants migration from pipes used in drinking water distribution systems: a review of the scientific literature. Environ. Sci. Pollut. Res. 29, 75134–75160. https://doi.org/10.1007/s11356-022-23085-7.

Multi-Resolution Land Characteristics Consortium. National land cover dataset (NLCD). https://search.library.wisc.edu/catalog/9910122133902121.

Munoz, G., Michaud, A.M., Liu, M., Vo Duy, S., Montenach, D., Resseguier, C., Watteau, F., Sappin-Didier, V., Feder, F., Morvan, T., Houot, S., Desrosiers, M., Liu, J., Sauvé, S., 2022. Target and nontarget screening of PFAS in biosolids, composts, and other organic waste products for land application in France. Environ. Sci. Tech. 56 (10), 6056–6068.

Murray, C.C., Vatankhah, H., McDonough, C.A., Nickerson, A., Hedtke, T.T., Cath, T.Y., Higgins, C.P., Bellona, C.L., 2019. Removal of per- and polyfluoroalkyl substances using super-fine powder activated carbon and ceramic membrane filtration. J. Hazard. Mater. 366, 160–168.

National Oceanic and Atmospheric Administration (NOAA). Coastal Change Analysis Program (C-CAP). 2022; National Oceanic and Atmospheric Administration Office for Coastal Management http://www.coast.noaa.gov/digitalcoast/data/ccapregion al/.

Neuwald, I.J., Hübner, D., Wiegand, H.L., Valkov, V., Borchers, U., Nödler, K., Scheurer, M., Hale, S.E., Arp, H.P.H., Zahn, D., 2022. Ultra-short-chain PFASs in the sources of german drinking water: prevalent, overlooked, difficult to remove, and unregulated. Environ. Sci. Tech. 56 (10), 6380–6390.

New Jersey Department of Environmental Protection. 2022a. New Jersey Private Well Testing Act. https://dep.nj.gov/dsr/oqa/pwta/.

New Jersey Department of Environmental Protection.2022b. PFAS in Drinking Water. https://www.nj.gov/dep/pfas/drinking-water.html.

Paul Friedman, K., Gagne, M., Loo, L.-H., Karamertzanis, P., Netzeva, T., Sobanski, T., Franzosa, J.A., Richard, A.M., Lougee, R.R., Gissi, A., Lee, J.-Y., Angrish, M., Dorne, J.L., Foster, S., Raffaele, K., Bahadori, T., Gwinn, M.R., Lambert, J., Whelan, M., Rasenberg, M., Barton-Maclaren, T., Thomas, R.S., 2020. Utility of in vitro bioactivity as a lower bound estimate of in vivo adverse effect levels and in risk-based prioritization. Toxicol. Sci. 173 (1), 202–225.

Post, G.B., Louis, J.B., Lippincott, R.L., Procopio, N.A., 2013. Occurrence of perfluorinated compounds in raw water from New Jersey public drinking water systems. Environ. Sci. Technol. 47, 13266–13275. https://doi.org/10.1021/es402884x.

Post, G.B., 2021. Recent US State and Federal Drinking Water Guidelines for Per- And Polyfluoroalkyl Substances (PFAS). Environmental Toxicology and Chemistry 2020; n/a10.1002/etc.4863.

Qian, S.S., Schulman, A., Koplos, J., Kotros, A., Kellar, P., 2004. A hierarchical modeling approach for estimating national distributions of chemicals in public drinking water systems. Environ. Sci. Tech. 38, 1176–1182. https://doi.org/10.1021/es020686q.

R Development Core Team. 2019. R: A Language and Environment for Statistical Computing. Version 3.5.2.

Richard, A.M., Judson, R.S., Houck, K.A., Grulke, C.M., Volarath, P., Thillainadarajah, I., Yang, C., Rathman, J., Martin, M.T., Wambaugh, J.F., Knudsen, T.B., Kancherla, J., Mansouri, K., Patlewicz, G., Williams, A.J., Little, S.B., Crofton, K.M., Thomas, R.S., 2016. ToxCast chemical landscape: paving the road to 21st century toxicology. Chem. Res. Toxicol. 29 (8), 1225–1251.

Romanok, K.M., Bradley, P.M., Meppelink, S.M., Kolpin, D.W., 2019. Mixed Organic and Inorganic Tapwater Exposures and Predicted Effects in the Greater Chicago Area, 2017. U.S. Geological Survey data release 10.5066/P9VOOBWT.

Romanok, K.M., Bradley, P.M., 2018a. Target-Chemical Concentration Results of Mixed-Organic/Inorganic Chemical Exposures in Puerto Rico Tapwater, 2018. 2021b; U.S. Geological Survey data release. 10.5066/P9EQS5CS.

Romanok, K.M., Bradley, P.M., LeBlanc, D.R., 2018b. Target-Chemical Concentration Results of Mixed-Organic/Inorganic Chemical Exposures in Cape Cod, Massachusetts Tapwater, 2018. 2020; U.S. Geological Survey data release. 10.5066/P9RKZK1E.

Romanok, K.M., Bradley, P.M., Smalling, K.L., Meppelink, S.M., McCleskey, R.B., Hladik, M.L., et al., 2023a. Target-Chemical Concentrations and Bioassay Results for Assessment of Mixed-Organic/Inorganic Chemical and Biological Exposures in Private-Well Tapwater at French Island, Wisconsin, 2021. U.S. Geological Survey data release 10.5066/P9EUBGUF.

Romanok, K.M., Smalling, K.L., Bradley, P.M., Meppelink, S.M., McCleskey, R.B., Hladik, M.L., et al., 2023b. Target-chemical concentrations and bioassay results for assessment of mixed-organic/inorganic chemical and biological exposures in Minneapolis/St Paul, Minnesota tapwater, August 2019. U.S. Geological Survey data release 10.5066/P9YQ24QW.

Romanok, K.M., Smalling, K.L., Bradley, P.M., McCleskey, B.R., Hladik, M.L., Gray, J.L., et al., 2022. Concentrations of organic and inorganic constituents in tapwater

samples from California in 2020-21 (ver. 3, September 2022). U.S. Geological Survey data release. doi: 10.5066/P9X3XLK3.

Romanok, K.M., Smalling, K.L., Bradley, P.M., Riddle, D.M., Kenefic, L.F., Gray, J.L., et al., 2023c. Concentrations of PFAS in tapwater collected throughout the United States, 2021-22. U.S. Geological Survey data release 10.5066/P9HIG9WI.

Romanok, K.M., Bradley, P.M., 2018. Target-Chemical Concentrations, Exposure Activity Ratios, and Bioassay Results for Assessment of Mixed-Organic/Inorganic-Chemical Exposure in USA Tapwater, 2016. U.S. Geological Survey data release. doi: 10.5066/F7959GVJ.

Romanok, K.M., Bradley, P.M. 2021. Target-Chemical Concentration Results of Mixed-Organic/Inorganic Chemical Exposures in Puerto Rico Tapwater, 2018. U.S. Geological Survey data release. https://doi.org/10.5066/P9EQS5CS.

Romanok, K.M., Kolpin, D.W., Meppelink, S.M., Argos, M., Brown, J.B., Devito, M.J., et al., 2018c. Methods used for the collection and analysis of chemical and biological data for the Tapwater Exposure Study, United States, 2016–17. Open-File Report 2018–1098. https://doi.org/10.3133/ofr20181098.

Salvatore, D., Mok, K., Garrett, K.K., Poudrier, G., Brown, P., Birnbaum, L.S., Goldenman, G., Miller, M.F., Patton, S., Poehlein, M., Varshavsky, J., Cordner, A., 2022. Presumptive contamination: a new approach to PFAS contamination based on likely sources. Environ. Sci. Technol. Lett. 9 (11), 983–990. https://doi.org/10.1021/acs.estlett.2c00502.

Schroeder, A.L., Ankley, G.T., Houck, K.A., Villeneuve, D.L., 2016. Environmental surveillance and monitoring—the next frontiers for high-throughput toxicology. Environ. Toxicol. Chem. 35, 513–525. https://doi.org/10.1002/etc.3309.

Seawolf, S.M., Williams, B.M., Gordon, S.E., Romanok, K.M., Smalling, K.L., Bradley, P.M., and Morriss, M.C., 2023. PFAS Reconnaissance Landscape Data: U.S. Geological Survey data release. https://doi.org/10.5066/P9JF1EXH.

Seltenrich, N., 2017. Unwell: the public health implications of unregulated drinking water. Environ. Health Perspect. 125, 114001. https://doi.org/10.1289/EHP2470.

Sepulvado, J.G., Blaine, A.C., Hundal, L.S., Higgins, C.P., 2011. Occurrence and fate of perfluorochemicals in soil following the land application of municipal biosolids. Environ. Sci. Tech. 45, 8106–8112. https://doi.org/10.1021/es103903d.

Sims, J.L., Stroski, K.M., Kim, S., Killeen, G., Ehalt, R., Simcik, M.F., Brooks, B.W., 2022. Global occurrence and probabilistic environmental health hazard assessment of per- and polyfluoroalkyl substances (PFASs) in groundwater and surface waters. Sci. Total Environ. 816, 151535. https://doi.org/10.1016/j.scitotenv.2021.151535.

Stalter, D., O'Malley, E., von Gunten, U., Escher, B.I., 2020. Mixture effects of drinking water disinfection by-products: implications for risk assessment. Environ. Sci. Water Res. Technol. 6, 2341–2351. https://doi.org/10.1039/C9EW00988D.

Stow, C.A., Webster, K.E., Wagner, T., Lottig, N., Soranno, P.A., Cha, Y., 2018. Small values in big data: the continuing need for appropriate metadata. Eco. Inform. 45, 26–30. https://doi.org/10.1016/j.ecoinf.2018.03.002.

Strynar, M., Dagnino, S., McMahen, R., Liang, S., Lindstrom, A., Andersen, E., McMillan, L., Thurman, M., Ferrer, I., Ball, C., 2015. Identification of Novel Perfluoroalkyl Ether Carboxylic Acids (PFECAs) and Sulfonic Acids (PFESAs) in Natural Waters Using Accurate Mass Time-of-Flight Mass Spectrometry (TOFMS). Environ. Sci. Tech. 49 (19), 11622–11630.

Strynar, M., 2017. Standard Operating Procedure: Method for Extraction and Analysis of Perfluoroethercarboxylic acids (PFECAs) from Surface Water, Well Water and Waste Water by Ultra-High Performance Liquid Chromatography (UPLC)-Tandem Mass Spectrometry (MS/MS). 2017; EPA D-EMMD-PHCB-062-SOP-01:26.

Sunderland, E.M., Hu, X.C., Dassuncao, C., Tokranov, A.K., Wagner, C.C., Allen, J.G., 2019. A review of the pathways of human exposure to poly- and perfluoroalkyl substances (PFASs) and present understanding of health effects. J. Eposure Sci. Environ. Epidemiol. 29, 131–147. https://doi.org/10.1038/s41370-018-0094-1.

Teymoorian, T., Munoz, G., Vo Duy, S., Liu, J., Sauvé, S., 2023. Tracking PFAS in drinking water: a review of analytical methods and worldwide occurrence trends in tap water and bottled water. ACS ES&T Water 3 (2), 246–261.

Tokranov, A.K., Bradley, P.M., Focazio, M.J., Kent, D.B., LeBlanc, D.R., McCoy, J.W., et al., 2021. Integrated science for the study of perfluoroalkyl and polyfluoroalkyl substances (PFAS) in the environment—A strategic science vision for the U.S. Geological Survey. 2021; U. S. Geological Survey Circular 1490:50 10.3133/cir1490.

U.S. Environmental Protection Agency, 2011. EPA's National-scale Air Toxics Assessment, An Overview of Methods for EPA's National-Scale Air Toxics Assessment. 2011; https://www.epa.gov/sites/production/files/2015-10/documents/2005-nata-tmd.pdf.

U.S. Environmental Protection Agency. Fifth Unregulated Contaminant Monitoring Rule. 2023a; https://www.epa.gov/dwucmr/fifth-unregulated-contaminant-monitoring-rule.

U.S. Environmental Protection Agency. Per- and Polyfluoroalkyl Substances (PFAS) Proposed PFAS National Primary Drinking Water Regulation. 2023b; https://www.epa.gov/sdwa/and-polyfluoroalkyl-substances-pfas.

U.S. Environmental Protection Agency. 2023c. Private drinking water wells. https://www.epa.gov/privatewells.

U.S. Environmental Protection Agency, 2012. Sustainable Futures / Pollution Prevention (P2) Framework Manual. EPA-748-B12-001:326 https://www.epa.gov/sustainable-futures/sustainable-futures-p2-framework-manual.

U.S. Environmental Protection Agency. 2022a. EPA's Drinking Water Health Advisories for PFOA and PFOS. https://www.epa.gov/sdwa/drinking-water-health-advisories-pfoa-and-pfos.

U.S. Environmental Protection Agency, 2022b. Third Unregulated Contaminant Monitoring Rule. https://www.epa.gov/dwucmr/third-unregulated-contaminant-monitoring-rule.

U.S. Environmental Protection Agency, 2022c. EPA's National Center for Computational Toxicology. ToxCast Database 3 (5). https://doi.org/10.23645/epacomptox.6062623.v8.

U.S. Environmental Protection Agency. 2020. A Review of the Reference Dose and Reference Concentration Process. https://www.epa.gov/osa/review-reference-dose-and-reference-concentration-processes.

Wang, Z., Cousins, I.T., Scheringer, M., Hungerbühler, K., 2013. Fluorinated alternatives to long-chain perfluoroalkyl carboxylic acids (PFCAs), perfluoroalkane sulfonic acids (PFSAs) and their potential precursors. Environ. Int. 60, 242–248. https://doi.org/10.1016/j.envint.2013.08.021.

Wang, Z., Cousins, I.T., Scheringer, M., Hungerbuehler, K., 2015. Hazard assessment of fluorinated alternatives to long-chain perfluoroalkyl acids (PFAAs) and their precursors: Status quo, ongoing challenges and possible solutions. Environ. Int. 75, 172–179. https://doi.org/10.1016/j.envint.2014.11.013.

Wu, R., Qian, S.S., Hao, F., Cheng, H., Zhu, D., Zhang, J., 2011. Modeling contaminant concentration distributions in China's centralized source waters. Environ. Sci. Tech. 45, 6041–6048. https://doi.org/10.1021/es1038563.

Zheng, Y., Flanagan, S.V., 2017. The case for universal screening of private well water quality in the U.S. and testing requirements to achieve it: Evidence from arsenic. Environ. Health Perspect. 125 (085002) https://doi.org/10.1289/EHP629.